

08/117,363


**UNITED STATES DEPARTMENT OF COMMERCE
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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/117,363 09/03/93 COOK

P ISIS1169

EXAMINER

18N1/1230

ART UNIT PAPER NUMBER

12

1807

DATE MAILED: 12/30/94

 JOSEPH LUCCI
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 This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 8/31/94 ☐ This action is made final.

 A shortened statutory period for response to this action is set to expire 3 month(s), — days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133
Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input checked="" type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> _____ |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-29 are pending in the application.
Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-29 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____, has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received
☒ been filed in parent application, serial no. PCT/US92/04116; filed on 10/23/92.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

BEST AVAILABLE COPY**EXAMINER'S ACTION**

15. The Information Disclosure Statement filed on 4/11/94 contains the following references which were not considered because no copy was furnished:

References AB, AF and AL.

Copies were not send because "it is believed to be too voluminous to send . . ." To have these references considered copies *must* be sent (MPEP 609). If the documents are too large than it is suggested that only those passages be sent which are considered most relevant.

16. Claim 16 is objected to for the informality of the phrase "having formula:". Amendment to "having the formula" is suggested.

17. Claims 1-29 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-29 recite " $N(R_{1a})(R_{1b})$," " $C(X)$ " and " $C(O)$ ". It is not clear how the atoms within the parentheses marks are bonded to the atoms outside the quotation marks, single bonds?, double bonds?, branching off from the main chain?, etc.

B. Claim 17-29 recite the "compound of claim 16" (or claim 28). "Compound" lacks antecedent basis in claim 16 which is

drawn to a nucleoside. Amendment to replace "compound" with "nucleoside" is suggested.

18. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, for failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification discloses, on page 5, lines 12-27, that the claimed compounds and nucleosides are to provide improvements diagnostic methods and materials for assaying "bodily states in animals, especially disease states" and "to provide therapeutic and research articles having improved transfer and uptake properties for the treatment of diseases through modulation of the activity of DNA or RNA. The specification examples show that cholic acid at the end of an oligomer does not effect T_m (p. 27, line 25) and increases cellular membrane transport (pp. 29-31, and p. 34). The specification examples also show that the addition of a 3' alkylamino group decreases nuclease resistance.

The specification does not show how to use the claimed compounds for the stated utility. Clearly, the claimed compounds

and oligonucleotides must maintain their ability to hybridize to a complementary nucleic acid to have utility. The claims are drawn to compounds in which the internucleoside linkages can vary widely in size and make up. The only examples in the specification utilize nucleic acid with the usual linkage or with a phosphorothioate linkage.

In order to function the synthetic oligonucleotide must be able to hybridize with its target, a complementary strand (see Stein et al. Science 261:1004, 8/20/93, Abstract, item (v)) In order to hybridize to a complementary strand, a synthetic oligonucleotide must have a structure similar to that complementary strand. For example, the distance from one base to the adjacent base on a strand must be the same on the synthetic oligonucleotide as on the complementary strand. Clearly, the vast majority of oligonucleotides within the scope of these claims would have a much larger distance from one base to the next. Lacking any further guidance from the specification as to which of the myriad possible linkages would have a functional base to base distance, the art skilled would be forced into the undue experimentation of constructing and testing the compounds for their ability to hybridize to complementary strands in order to enable a reasonable number of embodiments .

19. Claims 1-29 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 1-4, 6-18 and 20-29 are rejected under 35 U.S.C. § 102(b) as being anticipated by Matteucci et al. WO 92/05186 4/1/92 (Matteucci).

Claims 1 and 16 are drawn to compounds and nucleosides comprising a ribofuranosyl sugar bearing at a 2', 3' or 5'-O-position, a substituent having the formula, for example alkyl-N-.

Claims 2-4, 6-15, 17, 18 and 20-29 further limit the substituent of their respective base claims to recite: an alkyl chain of 1 to 10, for example 6, an alkyl chain including -C(O)-, -C(S)-, -C(O)-O-, and -O-(CH₂CH₂-O)_x.

Matteucci teaches these compounds and nucleosides having these substituents at 3' and 5'-O-positions, on page 13, line 2 to page 20 line 30, for example.

22. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject

matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

23. Claims 1-4, 6-18 and 20-29 are rejected under 35 U.S.C.

§ 103 as being unpatentable over Matteucci. In addition to embodiments that are anticipated by Matteucci, these claims also contain embodiments that are obvious over Matteucci. For example, these claims differ from Matteucci in the recitation of "a reporter enzyme." However, Matteucci teaches detection of base complementarity "which is then detected by conventional means. . . . radioactive, fluorescent, or chromogenic labels (Matteucci p. 24, lines 16-24)." It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use "a reporter enzyme" in place of the prior art teaching view of "radioactive, fluorescent, or

chromogenic labels" because the claimed enzyme and the prior art materials are art recognized alternative detectable labels.

24. Claims 5 and 19 are rejected under 35 U.S.C. § 103 as being unpatentable over Matteucci as applied to claim above, and further in view of applicants admissions.

Claims 5 and 19 further limit there respective base claims to recite a "phthalimido" side group. Applicant admits that this is known in the art at page 11, line 22 of the specification as a protecting group. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use phthalimido group to protect the amine groups during the organic synthesis process.

25. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Solomons, "Organic Chemistry," pub. 1980 by John Wiley & Sons pp. 818-819, illustrated reactions using Phthalimide.

26. Papers relating to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax center numbers are (703) 305-3014 or (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott Houtteman whose telephone number is (703) 308-3885. The examiner can normally be reached on Tuesday-Friday from 8:30 AM - 6:00 PM. The examiner can also be reached on alternate Mondays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Margaret Parr, can be reached at (703) 308-2454.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Scott Houtteman

Scott Houtteman
December 23, 1994

M. Parr 12/23/94

MARGARET PARR
SUPERVISORY PATENT EXAMINER
GROUP 1800